RESEARCH PROGRESS REPORT SUMMARY

Grant 02661: Investigation into Diet-Associated Dilated Cardiomyopathy in Dogs

Principal Investigator: Darcy Adin, DVM

Research Institution: University of Florida

Grant Amount: $211,521.24

Start Date: 4/1/2019 **End Date:** 3/31/2025

Progress Report: End-Year 5

Report Due: 3/31/2024 **Report Received:** 3/22/2024

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Original Project Description:

Dilated cardiomyopathy (DCM) is a serious disease of the heart muscle whereby the heart becomes enlarged with weak contractions. DCM can result in abnormal heart rhythms, congestive heart failure or sudden death. In dogs, DCM most often occurs in large- and giant-breeds, such as Doberman Pinschers, Boxers, Irish Wolfhounds, and Great Danes; in these dogs, survival time after diagnosis is often only months, even with aggressive medical therapy. Recently, veterinary cardiologists have recognized DCM more frequently in all breeds of dogs including mixed breeds, and even those not usually associated with DCM. There is suspicion that the disease in some dogs is associated with boutique, exotic ingredient, or grain-free (BEG) diets. Some affected dogs on such diets have shown reversal or improvement of their disease after changing their diet, supporting a potential association between consumption of a BEG diet and development of DCM. A specific cause, however, has not been identified, despite extensive nutritional testing of the dog foods and the canine patients. Moreover, the extent of the problem is unknown because only dogs that are symptomatic for DCM have been reported. It is possible that more dogs may be affected but not yet showing signs of heart disease. To investigate the extent of diet-associated heart problems in dogs, this multi-institutional team of veterinary cardiologists and nutritionists will prospectively screen a large population of apparently healthy dogs for DCM and compare important cardiac disease measures, including ultrasound of the heart, blood biomarker and taurine concentrations, and the frequency of DCM in dogs eating BEG versus non-BEG diets.

Publications:

Adin, Darcy B., and Jorge A. Hernandez. “Influence of Sex on Renin-Angiotensin-Aldosterone System Metabolites and Enzymes in Doberman Pinschers.” Journal of Veterinary Internal Medicine 37, no. 1 (2023): 22–27. https://doi.org/10.1111/jvim.16589.

Adin D, Freeman L, Stepien R, Rush J, Tjostheim S, Kellihan H, Aherne M, Vereb M, Goldberg R. Effect of Diet Type on Circulating Taurine Concentrations, Cardiac Biomarkers, and Echocardiograms in Four Dog Breeds. J Vet Intern Med, 2021:35(2):771-779. doi.org/10.1111/jvim.16075.

Haimovitz D, Vereb M, Freeman L, Goldberg R, Lessard D, Rush J, Adin D. Effect of diet change in healthy dogs with subclinical cardiac biomarker or echocardiographic abnormalities. J Vet Intern Med 2022:36:1057–1065. doi: 10.1111/jvim.16416

Adin D, Haimovitz D, Freeman LM, Rush JE. Untargeted global metabolomic profiling of healthy dogs based on grain-inclusivity of diet. American Journal of Veterinary Research 83(9):1-9 3/25/2022. doi: 10.2460/ajvr.22.03.0054

Stepien RL1, Kellihan HB1, Visser LC2, Wenholz L1, Luis Fuentes V3, Echocardiographic values for normal conditioned and unconditioned North American whippets. Journal of Veterinary Internal Medicine, Published 28 Mar 2023, DOI: 10.1111/jvim.16691 PMID: 36975003 https://europepmc.org/article/med/36975003

Brethel S, Locker S, Girens R, Rivera P, Meurs K, Adin D. The effect of taurine supplementation on the renin–angiotensin–aldosterone system of dogs with congestive heart failure. Sci Rep. 2023;13(1):10700. doi:10.1038/s41598-023-37978-1

Presentations:

Adin D. “Puzzling out the nutritional DCM issue in the US” April 23, 2021 (virtual), CE provided to the Veterinary Cardiovascular Society in the UK

Haimovitz D, Adin D, Freeman L, Goldberg R, Vereb M, Rush J. Effect of Diet Change in Healthy Dogs with Subclinical Cardiac Biomarker or Echocardiographic Abnormalities. AKC CHF Parent Conference (virtual poster) Aug 14, 2021.

Adin D. “Puzzling out the nutritional DCM issue” Nov 13, 2022, Florida Veterinary Medical Association, Panama City Beach, FL

Haimovitz D, Adin D, Freeman L, Goldberg R, Vereb M, Rush J. Effect of Diet Change in Healthy Dogs with Subclinical Cardiac Biomarker or Echocardiographic Abnormalities. University of Florida Top Dog Competition (awarded the winner of the class of 2022)

Sewell, T, Fan T, Adin D. An Enzyme-linked Immunosorbent Assay for the Detection of Phytohemagglutinin in Legumes. June 2023 ACVIM Forum (poster), Philadelphia, PA.

Report to Grant Sponsor from Investigator:

The study titled "Investigation into Subclinical Diet-Associated Dilated Cardiomyopathy in Four Dog Breeds" has resulted in 4 peer-reviewed manuscripts published in the Journal of Veterinary Internal Medicine, the American Journal of Veterinary Research and Scientific Reports.

The results of this work demonstrated higher levels of cardiac troponin I in dogs eating grain-free (GF) dog foods or foods that have peas, lentils or potatoes in the top 10 ingredients compared to dogs eating grain-inclusive (GI) dog foods or foods without peas, lentils, or potatoes in the top 10 ingredients. Cardiac troponin I is a blood marker that indicates injury to the heart muscle and therefore this study provides information on how heart disease occurs in some dogs eating GF diets. Additionally, we showed that cardiac troponin I decreased, and an echocardiographic (ultrasound of the heart) measure of contractility improved in dogs fed GF diets that were changed to a GI diet without peas or lentils 1 year after this diet change. This is important information because it shows that apparently healthy dogs can have subtle heart muscle injury that can improve with diet change. Therefore, this data is supportive of causation.

We also analyzed the blood of enrolled dogs to study small molecules indicative of metabolic pathways in the body. We found many differences between dogs eating GF diets compared to dogs eating GI diets and specifically found key differences in lipid and amino acid metabolism which were largely eliminated 1 year after diet change. Several unnamed compounds were identified as differentiators of diet type which will require more study before deciding if they are clinically important. Although the data from this aspect of the study did not reveal specific biochemical changes that are responsible for myocardial injury, it did highlight the marked differences that occur in the body as a result of food that is ingested. These different biochemical pathways in the blood might provide insight into underlying mechanisms supportive of disease propagation.

Our investigation into the effect of taurine on the renin-angiotensin-aldosterone system (RAAS) did not provide strong evidence that taurine is helping dogs with diet-associated DCM through suppression of the RAAS. Some dogs, however, did respond, especially those that were recently hospitalized and had high RAAS levels to begin with. Therefore, it is possible that it helps some dogs, but this area will require further study to determine if there might be other ways that taurine can benefit this disease when deficiency is not present.

We also utilized stored serum from this study to determine if there was evidence of phytohemagglutinins in the blood of study dogs and in both grain-free, high-legume and grain-inclusive, legume-free dog foods. Legumes contain phytohemagglutinins that can cause red blood cell

clumping if improperly processed. Evaluation of grain-free dog foods showed that some had higher phytohemagglutinin concentrations than other grain-free ones, and higher than grain-inclusive foods that were tested, however, what constitutes a clinically important level is unknown. This data was presented at the 2023 ACVIM Forum. Several stored serum samples from dogs eating grain-free food and grain-inclusive foods and several clinically affected dogs were also evaluated. Results were not significantly different between groups.

The Principal Investigator requested and was awarded a no-cost extension with a new project end date of March 31, 2025